IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN REAPPLICATION OF: Aleardo Koverech

GROUP ART UNIT: 1617 SERIAL NO.: 10/535,509

EXAMINER: Timothy E. Betton FILED: 05/18/2005

FOR: USE OF CARNITINES FOR THE PREVENTION AND/OR TREATMENT OF DISORDERS CAUSED BY THE ANDROPAUSE

DECLARATION UNDER 37 C.F.R. §1.132

ASSISTANT COMMISSIONER FOR PATENTS

WASHINGTON, D.C. 20231

SIR:

I, Aleardo Koverech,

a citizen of Italy

residing at: Aurelia Antica, 200 – I-00165 Rome Italy,

hereby declare as follows:

1. That I am a graduate in Medicine and Surgery, University of Rome.
2. That I have been employed by Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., the assignee of the above-identified application since 1979, and since 2000 I am Director, Nutraceutical Products and Strategic Development of Carnitine in Europe, Sigma-Tau Pharmaceuticals.
3. That I am familiar with the contents of this application as well as the underlying research efforts, the Official Action of January 28, 2008 and the prior art documents cited in it.
4. That I am familiar with the attached studies, that I participated in the studies and am familiar with the objectives, design, components employed and the results obtained was conducted under my supervision and control.

That upon information and belief the data included in the attached are accurate.

THREE-MONTH THERAPY:

Patients were selected according to the same criteria described in the application N. 10/535509.

Group 1 was treated with acetyl L-carnitine, 4 g/day, Group 2 was treated with propionyl L-carnitine 4 g/day. No placebo Group was present. 10 patients for each group.

Data are summarized in the following Table. In the last column the data shown in the application for the claimed combination are shown.

Mean age: 63 ± 2.2 (range 61-66) for Group 1

64 ± 2.3 (range 61-67) for Group 2.

No side effects were recorded.

Statistical analysis was done with ANOVA, with the exclusion of score of IIEF 15, DMS and fatigue, which used FRIEDMAN non parametric test.

S.D. = standard deviation.

PSV = Peak Sistolic Velocity of right cavernous artery. Left cavernous artery gave similar results.

EDV = End Diastolic Velocity of right cavernous artery. Left cavernous artery gave similar results.

RI = Resistance Index of right cavernous artery. Left cavernous artery gave similar results.

NPT = Nocturnal Erection Duration.

IIEF 15: International Index of Erectile Function.

DMS = Depression/melancholia scale.

Measured Variable		Pre-therapy		After three months therapy		
		Group 1	Group 2	Group 1	Group 2	combination of the invention
PSA tot ng/ml mean ± S.D.		1,83±0,8	1.76±0,65	1,77±0,7	1,77±0,6	2.21±0.654
Volume prostate cm^3 mean ± S.D.		14,5±2,6	15,0±1,9	14,6±2,6	14,8±2,4	14.5±2.6
PSV cm/sec mean ± S.D. Right cavernous artery		28.9±1.7	29.4±2.2	32.2±2.2	33.2±2.1	33.9±4.2
PSV cm/sec mean ± S.D. Left cavernous artery		Results similar to the Right cavernous artery				
EDV cm/sec mean ± S.D. Right cavernous artery		14.2±2.3	14.5±2.4	6.4±2.2	7.3±2.0	7.1±3.8
EDV cm/sec mean ± S.D. Left cavernous artery		Results similar to the Right cavernous artery				
RI% mean ± S.D. Right cavernous artery		50.7±8.4	50.3±11.3	60.4±3,8	61,2±6,0	63.7±7.4
RI% mean ± S.D. Left cavernous artery		Results similar to the Right cavernous artery				
NPT minutes mean ± S.D.		85±9	82±7	132±10	135±13	112.8 ± 16.1
Total Testosterone nmol mean ± S.D. /l		9.45±0.04	9.26±0.04	9.56±2.7	9.14±2.2	15.2±3.0
Free Testosterone pg/ml mean ± S.D.		5.38±0.3	5.38±0.3	5.41±0.3	5.45±0.3	4.5±1.1
LH IU/L mean ± S.D.		8.2±0.3	7.9±0.2	8.3±0.2	8.0±0.3	8.5±0.7
Prolactin ng/ml mean ± S.D.		7.5±0.3	7.5±0.4	7.6±0.3	7.5±0.2	7.4±1.9
IIEF 15 Score median (range)	Erectile Function	7(6-20)	8 (6-20)	12 (7-27)	13 (7-28)	16.7±5.4
	Sexual Intercourse Satisfaction	4 (3-6)	4 (3-6)	5 (4-8)	6 (4-8)	5.3±1.2
	Orgasm	3 (2-5)	3 (2-4)	5 (4-8)	6 (4-8)	5.4±1.3
	Sexual desire	3 (2-4)	3 (2-4)	6 (4-8)	5 (4-8)	6.6±1.3
	General wellness	3 (2-5)	3 (2-5)	5 (4-8)	5 (4-8)	5.2±1.5
DMS III median (range)		7 (5-8)	6 (4-8)	5 (2-6)	5 (3-6)	4.7±0.9
Fatigue scale mediana (range)		3 (1-6)	3 (1-5)	1 (0-4)	1 (0-4)	1.3±1.1

Unchanged variables are not shown.

The following variables changed.

PSV

Group 1 significantly lower pre- vs therapy $F = 42.6$; $p<0.01$

Group 2 significantly lower pre- vs therapy $F = 20.4$, $p<0.01$

There are no significant differences between the two groups during therapy. After three months, data from these groups are significantly lower than the group treated with ALC+PLC, as disclosed in the application in re. (F respectively = 11.2 and 12.7; $p<0.01$ in each case).

EDV

Group 1 is significantly higher pre- vs therapy $F = 42.6$ $p<0.01$

Group 2 is significantly higher pre- vs therapy $F = 45.0$ $p<0.01$

There are no significant differences between the two groups during therapy. After three months, data from these groups are significantly higher than the group treated with ALC+PLC, as disclosed in the application in re. (F respectively = 6.7 and 7.0; $p<0.05$ and 0.01 in each case).

RI

Group 1 is significantly lower pre- vs therapy $F = 13.2$; $p<0.01$

Group 2 is significantly lower pre- vs therapy $F = 18,3$; $p<0.01$

There are no significant differences between the two groups during therapy. After three months, data from these groups are significantly lower than the group treated with ALC+PLC, as disclosed in the application in re. (F respectively = 8,9 and 9,9; $p<0.01$ in each case).

NPT

Group 1 significantly lower pre- vs therapy $F = 15.4$; $p<0.01$

Group 2 significantly lower pre- vs therapy $F = 9.9$; $p<0.01$

There are no significant differences between the two groups during therapy. After three months, data from these groups are significantly lower than the group treated with ALC+PLC, as disclosed in the application in re. (F respectively = 12.3 and 10.1; $p<0.01$ in each case)

IIEF15: erectile function

Group 1 significantly lower pre- vs therapy $q = 14.2$; $p<0.01$

Group 2 significantly lower pre- vs therapy $q = 13.8$; $p<0.01$

There are no significant differences between the two groups during therapy. After three months, data from these groups are significantly lower than the group treated with ALC+PLC, as disclosed in the application in re. (q respectively = 11.2 and 12.1; $p<0.01$ in each case).

For the remaining parameters of the IIEF 15 there is a trend similar to the one observed for the erectile function.

Same consideration is for DMS and fatigue scale.

6 MONTHS THERAPY

No side effects were recorded.

Tables 1a-20a mentioned above comprise 5 treatment groups.

Groups 1, 2 and 5 relate to the experimental data present in the application as filed.

In Groups 3 and 4, the results *"Before therapy"* and *"During therapy (3 mos)"* relates to the data filed on March 2007 mentioned above; the data *"During therapy (6 mos)"* relates to the data now filed in response to the pending Communication (08.06.2007).

Please be informed that on Table 5a Groups 2 and 3, *"Before therapy"* the data filed on March 2007 which are *12.4 ± 2.3* and *14.5 ± 2.4* respectively, are not correct because of a typing error; the correct data are *7.5 ± 2.1* and *7.2 ± 2.3* respectively.

TABLE 1a

Mean serum levels of total prostate-specific antigen (PSA) ng/ml before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	**Type of therapy**	**Observation time**	**PSA ng/m**
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	2.02 ± 0.74
		During therapy (3 mos)	2.01 ± 0.79
		After therapy (6 mos)	2.02 ± 0.85
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	2.36 ± 0.87
		During therapy (3 mos)	2.21 ± 0.654
		After therapy (6 mos)	2.33 ± 0.77
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	1.83 ± 0.80
		During therapy(3 mos)	1.77 ± 0.70
		After therapy (6 mos)	1.88 ± 0.86
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	1.76 ± 0.65
		During therapy (3 mos)	1.77 ± 0.60
		After therapy (6 mos)	1.90 ± 0.88
5	Placebo	Before therapy	1.80 ± 0.77
		During therapy (3 months)	1.75 ± 0.75
		After therapy (6 mos)	1.75 ± 0.75

The results reported in Table 1a indicate that the treatment with the compound tested did not significantly increase blood PSA levels.

TABLE 2a

Mean prostate volume (cm^3) as measured by suprapubic ultrasonography and calculation of the three diameters, before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Prostate volume (cm3)
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	15.3 ± 2.8
		During therapy(3 mos)	15.5 ±3.0
		After therapy (6 mos)	15.5 ± 2.6
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	15.2 ± 2.7
		During therapy (3 mos)	14.5 ± 2.6
		After therapy (6 mos)	15.1 ± 3.1
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	14.5 ± 2.6
		During therapy (3 mos)	14.6 ± 2.6
		After therapy (6 mos)	15.3 ± 2.2
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	15.0 ± 1.9
		During therapy (3 mos)	14.8 ± 2.4
		After therapy (6 mos)	15.4 ± 1.9
5	Placebo	Before therapy	15.6 ± 3.2
		During therapy (3 mos)	15.5 ± 3.4
		After therapy (6 mos)	15.6 ± 3.3

The results reported in Table 2a indicate that the treatment with the compound tested did not significantly increase prostate volume.

TABLE 3a

Peak systolic velocity (PSV) (mean value in cm/sec) of the right cavernous artery of the penis as measured by dynamic colour Doppler ultrasonography before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Right cavernous artery PSV (cm/sec)
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	33.2 ± 3.9
		During therapy (3 mos)	32.8 ± 4.2
		After therapy (6 mos)	33.7 ± 3.7
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	33.9 ± 3.2
		During therapy (3 mos)	33.9 ± 3.2
		After therapy (6 mos)	33.9 ± 3.3
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	28.9 ± 1.7
		During therapy (3 mos)	32.2 ± 2.2
		After therapy (6 mos)	31.1 ± 1.4
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	29.4 ± 2.2
		During therapy (3 mos)	33.2 ± 2.1
		After therapy (6 mos)	31.4 ± 1.8
5	Placebo	Before therapy	33.7 ± 4.3
		During therapy (3 mos)	33.9 ± 5.0
		After therapy (6 mos)	33.8 ± 4.7

The results presented in Table 3a indicate that the treatment with the compounds tested did not induce significant changes.

Similar results emerged on measuring the PSV of the left cavernous artery; the results obtained, presented in Table 4a, show, in fact, that the treatment did not induce any significant changes.

TABLE 4a

Peak systolic velocity (PSV) (mean value in cm/sec) of the left cavernous artery of the penis as measured by dynamic colour Doppler ultrasonography before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Left cavernous PSV (cm/sec)
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	33.6 ± 3.7
		During therapy (3 mos)	32.6 ± 4.2
		After therapy (6 mos)	33.5 ± 3.5
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	34.1 ± 3.3
		During therapy (3 mos)	34.2 ± 3.3
		After therapy (6 mos)	34.1 ± 3.5
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	32.6 ± 1.9
		During therapy (3 mos)	31.2 ± 4.4
		After therapy (6 mos)	30.5 ± 1.1
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	29.9 ± 1.8
		During therapy (3 mos)	32.5 ± 2.3
		After therapy (6 mos)	31.7 ± 1.9
5	Placebo	Before therapy	33.4 ± 4.0
		During therapy (3 mos)	32.5 ± 4.8
		After therapy (6 mos)	32.7 ± 4.9

The results presented in Tables 5a, 6a, 7a and 8a here below show that the treatments administered also induced no significant differences either in the case of the other vascular parameters (EDV and RI) or as affecting the right or left cavernous arteries.

TABLE 5a

End-diastolic velocity (EDV) (mean value in cm/sec) of the right cavernous artery of the penis as measured by dynamic colour Doppler ultrasonography before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Right cavernous artery EDV (cm/sec)
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	7.8 ± 3.6
		During therapy (3 mos)	7.9 ± 3.6
		After therapy (6 mos)	7.9 ± 3.6
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	6.8 ± 3.6
		During therapy (3 mos)	7.1 ± 3.8
		After therapy (6 mos)	6.9 ± 3.6
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	7.5 ± 2.1
		During therapy (3 mos)	6.4 ± 2.2
		After therapy (6 mos)	8.6 ± 4.0
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	7.2 ± 2.3
		During therapy (3 mos)	7.3 ± 2.0
		After therapy (6 mos)	8.8 ± 4.4
5	Placebo	Before therapy	6.5 ± 3.8
		During therapy (3 mos)	6.7 ± 4.0
		After therapy (6 mos)	6.7 ± 4.3

TABLE 6a

End-diastolic velocity (EDV) (mean value in cm/sec) of the left cavernous artery of the penis as measured by dynamic colour Doppler ultrasonography before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Left cavernous artery EDV (cm/sec)
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	7.7 ± 3.5
		During therapy (3 mos)	7.5 ± 3.3
		After therapy (6 mos)	7.4 ± 3.3
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	6.4 ± 3.6
		During therapy (3 mos)	6.4 ± 3.3
		After therapy (6 mos)	6.5 ± 3.2
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	8.2 ± 2.3
		During therapy (3 mos)	6.4 ± 2.2
		After therapy (6 mos)	8.6 ± 3.4
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	7.9 ± 2.3
		During therapy (3 mos)	7.3 ± 2.0
		After therapy (6 mos)	7.9 ± 4.2
5	Placebo	Before therapy	6.9 ± 3.8
		During therapy (3 mos)	6.3 ± 3.8
		After therapy (6 mos)	6.2 ± 3.8

TABLE 7a

Resistance Index (RI) (%) of right cavernous artery before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data used were values subjected to angular transformation ($\sin^{-1} \sqrt{P/100}$) and presented as mean ± standard deviation.

Group	Type of therapy	Observation time	Right cavernous artery RI %
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	64.6 ± 8.4
		During therapy (3 mos)	60.9 ± 8.4
		After therapy (6 mos)	61.1 ± 7.9
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	64.2 ± 7.4
		During therapy (3 mos)	63.7 ± 7.4
		After therapy (6 mos)	64.1 ± 7.3
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	50.7 ± 8.4
		During therapy (3 mos)	60.4 ± 3.8
		After therapy (6 mos)	54.5 ± 7.0
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	50.3 ± 11.3
		During therapy (3 mos)	61.2 ± 6.0
		After therapy (6 mos)	52.0 ± 8.9
5	Placebo	Before therapy	64.5 ± 8.8
		During therapy (3 mos)	64.4 ± 9.2
		After therapy (6 mos)	64.7 ± 9.9

TABLE 8a

Resistance Index (RI) (%) of left cavernous artery before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data used were values submitted to angular transformation ($\sin^{-1}\sqrt{P/100}$) and presented as means ± standard deviation.

Group	Type of therapy	Observation time	Left cavernous artery RI %
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	61.5 ± 8.3
		During therapy (3 mos)	61.5 ± 7.8
		After therapy (6 mos)	62.1 ± 7.0
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	64.8 ± 6.8
		During therapy (3 mos)	64.9 ± 7.0
		After therapy (6 mos)	64.7 ± 7.0
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	52.7 ± 7.6
		During therapy (3 mos)	56.7 ± 4.3
		After therapy (6 mos)	55.5 ± 5.6
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	52.4 ± 4.3
		During therapy (3 mos)	63.3 ± 4.2
		After therapy (6 mos)	53.1 ± 5.5
5	Placebo	Before therapy	63.3 ± 8.7
		During therapy (3 mos)	64.6 ± 9.6
		After therapy (6 mos)	64.7 ± 8.7

TABLE 9a

Duration of full erections (in minutes) in the course of a recording period of three nights by Rigiscan before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Duration of full erections (in minutes)
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	108.3 ± 18.7
		During therapy (3 mos)	112.7 ± 21.1
		After therapy (6 mos)	119.6 ± 26.0
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	98.9 ± 18.5
		During therapy (3 mos)	112.8 ± 16.1
		After therapy (6 mos)	136.9 ± 28.1
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	85 ± 9.0
		During therapy (3 mos)	132 ± 10
		After therapy (6 mos)	89.4 ±6.0
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	82 ± 7.0
		During therapy (3 mos)	135 ± 13
		After therapy (6 mos)	90.2 ± 14
5	Placebo	Before therapy	105.3 ± 21.2
		During therapy (3 mos)	107.7 ± 21.2
		After therapy (6 mos)	102.6 ± 22.9

Table 9a presents the data for duration of full nocturnal erections in minutes recorded by Rigiscan for a period of 3 nights before, during and after therapy with the combination according to the invention, with testosterone and with placebo. The combination according to the invention (Group 2) induced a significant increase in duration of full nocturnal erections both at 3 ($F = 11.6$; $P < 0.01$) and at 6 months ($F = 19.1$; $P < 0.01$), while the administration of testosterone (Group 1) induced a significant increase in duration of full nocturnal erections at 6 months ($F = 12.4$, $P < 0.01$), but not at 3 months ($F = 1.01$; P = n.s.).

The duration of the nocturnal erections was greater after 6 months in the group treated with the combination according to the invention ($F = 4.2$, $P < 0.05$) than that of those observed after 6 months in the group treated with testosterone. The administration of placebo (Group 5) had no effect on the duration of full nocturnal erections ($F = 2.4$, P = n.s.).

In addition, using acetyl L-carnitine or propionyl L-carnitine alone (Groups 3 and 4) the increase of the nocturnal erections was observed only after 3 months, this effect was not confirmed after 6 months of treatment.

TABLE 10a

Blood levels of total testosterone before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Total testosterone nmol/l
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	14.5 ± 2.1
		During therapy (3 mos)	15.5 ± 3.9
		After therapy (6 mos)	15.8 ± 2.6
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	15.9 ± 2.8
		During therapy (3 mos)	15.2 ± 3.0
		After therapy (6 mos)	15.8 ± 4.4
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	9.4 ± 0.04
		During therapy (3 mos)	9.5 ± 2.7
		After therapy (6 mos)	9.5 ± 2.4
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	9.2 ± 0.04
		During therapy (3 mos)	9.1 ± 2.2
		After therapy (6 mos)	9.6 ± 2.7
5	Placebo	Before therapy	14.9 ± 2.0
		During therapy (3 mos)	14.8 ± 2.3
		After therapy (6 mos)	14.9 ± 1.9

Table 10a presents the data for blood total testosterone levels before, during and after therapy with the combination according to the invention (Group 2); testosterone (Group 1); placebo (Group 5); acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4). The treatment with the compounds tested induced no significant changes either 3 or 6 months.

Very similar results were obtained on analysing free blood testosterone during treatment with the compounds tested, the results obtained are presented in Table 11a.

TABLE 11a

Blood levels of free testosterone before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Free blood testosterone pg/ml
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	4.4 ± 0.8
		During therapy (3 mos)	19.5 ± 4.2
		After therapy (6 mos)	19.7 ± 4.0
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	4.6 ± 1.0
		During therapy (3 mos)	4.5 ± 1.1
		After therapy (6 mos)	4.5 ± 0.8
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	5.3 ± 0.3
		During therapy (3 mos)	5.4 ± 0.3
		After therapy (6 mos)	5.4 ± 0.7
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	5.3 ± 0.3
		During therapy (3 mos)	5.4 ± 0.3
		After therapy (6 mos)	5.5 ± 0.8
5	Placebo	Before therapy	4.2 ± 0.6
		During therapy (3 mos)	4.3 ± 0.8
		After therapy (6 mos)	4.1 ± 0.7

TABLE 12a

Blood levels of LH before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	LH IU/l
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	8.9 ± 0.6
		During therapy (3 mos)	4.3 ± 0.6
		After therapy (6 mos)	4.2 ± 1.2
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	8.4 ± 0.9
		During therapy (3 mos)	8.5 ± 0.7
		After therapy (6 mos)	8.5 ± 0.8
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	8.2 ± 0.3
		During therapy (3 mos)	8.3 ± 0.2
		After therapy (6 mos)	8.6 ± 0.7
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	7.9 ± 0.2
		During therapy (3 mos)	8.0 ± 0.3
		After therapy (6 mos)	8.5 ± 0.8
5	Placebo	Before therapy	8.7 ± 0.6
		During therapy (3 mos)	8.6 ± 0.6
		After therapy (6 mos)	8.7 ± 0.5

Table 12a presents the data for blood levels of LH before, during and after treatment with the tested compounds.

In particular, treatment with the combination according to the invention (Group 2); placebo (Group 5); acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) induced no significant changes in LH either at 3 or at 6 months. In contrast, the administration of testosterone led to a statistically significant reduction in blood levels of LH at 3 months, and a significant reduction at 6 months.

TABLE 13a

Blood prolactin levels before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Prolactin mcg/ml
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	7.7 ± 1.6
		During therapy (3 mos)	7.4 ± 1.7
		After therapy (6 mos)	7.3 ± 1.8
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	7.6 ± 1.9
		During therapy (3 mos)	7.4 ± 1.9
		After therapy (6 mos)	7.5 ± 2.2
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	7.5 ± 0.3
		During therapy (3 mos)	7.6 ± 0.3
		After therapy (6 mos)	7.8 ± 0.8
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	7.5 ± 0.4
		During therapy (3 mos)	7.5 ± 0.2
		After therapy (6 mos)	7.6 ± 0.8
5	Placebo	Before therapy	7.4 ± 1.7
		During therapy (3 mos)	7.7 ± 1.7
		After therapy (6 mos)	7.3 ± 1.8

The results reported in Table 13a indicate that the treatment with the compound tested did not significantly increase blood prolactin levels.

TABLE 14a

Scores on the International Index of Erectile Function questionnaire (IIEF-15) – "Erectile Function" section before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Score
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	13.8 ± 2.7
		During therapy (3 mos)	16.7 ± 3.7
		After therapy (6 mos)	20.2 ± 5.3
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	11.4 ± 5.4
		During therapy (3 mos)	16.7 ± 5.4
		After therapy (6 mos)	21.9 ± 7.3
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	8.8 ± 4.4
		During therapy (3 mos)	12.5 ± 4.8
		After therapy (6 mos)	9.1± 5.0
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	7.9 ± 3.7
		During therapy (3 mos)	13.3 ± 4.4
		After therapy (6 mos)	9.2 ± 3.7
5	Placebo	Before therapy	13.8 ± 1.1
		During therapy (3 mos)	12.9 ± 2.0
		After therapy (6 mos)	14.2 ± 2.9

The results reported in Table 14a indicate that the scores on the International Index of Erectile Function questionnaire (IIEF-15) – "Erectile Function" section, before, during and after therapy with the combination according to the invention (Group 2); testosterone (Group 1); placebo (Group 5); acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4). The combination according to the invention and testosterone induced a significant increase in scores both at 3 months ($F = 31.5$, $P < 0.01$ and $F = 6.3$, $P < 0.05$, respectively) and at 6 months ($F = 18.9$, $P < 0.01$ and $F = 29.2$, $P < 0.01$, respectively). Administration of the placebo (Group 5) acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) induced no significant changes in scores.

TABLE 15a

Scores on the "Intercourse Satisfaction" section before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Score
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	4.1 ± 0.8
		During therapy (3 mos)	4.8 ± 0.8
		After therapy (6 mos)	5.8 ± 1.9
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	4.6 ± 1.0
		During therapy (3 mos)	5.3 ± 1.2
		After therapy (6 mos)	6.9 ± 2.5
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	4.8 ± 2.1
		During therapy (3 mos)	4.9 ± 1.9
		After therapy (6 mos)	5.0 ± 2.0
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	4.4±3.0
		During therapy (3 mos)	5.8 ± 3.7
		After therapy (6 mos)	4.6 ± 2.7
5	Placebo	Before therapy	3.9 ± 0.8
		During therapy (3 mos)	4.3 ± 0.8
		After therapy (6 mos)	4.1 ± 0.7

Very similar results were obtained in the "Intercourse Satisfaction" (Table 15a) and "Sexual Desire" sections (Table 16a).

These results, too, indicate that the combination according to the invention (Group 2) and oral testosterone (Group 1) significantly increased intercourse satisfaction and sexual desire.

Administration of the placebo (Group 5) acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) induced no significant changes in scores.

TABLE 16a

Scores on the International Index of Erectile Function questionnaire (IIEF-15) – "Sexual Desire" section before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Score
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	4.3 ± 1.0
		During therapy (3 mos)	5.7 ± 0.8
		After therapy (6 mos)	7.1 ± 0.9
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	3.9 ± 0.8
		During therapy (3 mos)	6.6 ± 1.3
		After therapy (6 mos)	7.3 ± 1.9
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	3.4 ± 2.0
		During therapy (3 mos)	5.9 ± 2.7
		After therapy (6 mos)	4.7 ± 2.8
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	3.6± 3.0
		During therapy (3 mos)	5.3 ± 3.6
		After therapy (6 mos)	4.0± 2.2
5	Placebo	Before therapy	3.3 ± 0.9
		During therapy (3 mos)	3.3 ± 0.9
		After therapy (6 mos)	3.5 ± 0.5

TABLE 17a

Scores on the International Index of Erectile Function questionnaire (IIEF-15) – "Orgasmic Function" section before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Score
1	Testosterone undecaonate 40 x 2mg/day	Before therapy	3.2 ± 1.2
		During therapy (3 mos)	3.9 ± 0.9
		After therapy (6 mos)	4.7 ± 1.8
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	3.7 ± 1.1
		During therapy (3 mos)	5.4 ± 1.3
		After therapy (6 mos)	7.2 ± 1.1
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	3.2 ± 2.7
		During therapy (3 mos)	5.0 ± 2.6
		After therapy (6 mos)	4.4 ± 1.9
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	3.2 ± 1.9
		During therapy (3 mos)	6.0 ± 1.8
		After therapy (6 mos)	4.0 ± 2.5
5	Placebo	Before therapy	2.9 ± 0.7
		During therapy (3 mos)	3.4 ± 1.6
		After therapy (6 mos)	3.0 ± 0.6

The results reported in Table 17a indicate that the scores on the International Index of Erectile Function questionnaire (IIEF-15) – "General Satisfaction" section, before, during and after therapy with the combination according to the invention (Group 2); testosterone (Group 1); placebo (Group 5); acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4). The treatment induced significant changes; in particular, the combination according to the invention significantly increased the scores at 3 months ($F = 33.3$ $P < 0.01$) and at 6 months ($F = 33.6$, $P < 0.01$). The administration of testosterone, acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) or placebo (Group 5) failed to induce any significant changes in scores.

These results indicate that the combination according to the invention (Group 2) is significantly more active than testosterone (Group 1) acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) or placebo (Group 5) in increasing the general well-being (coenaesthesia) of patients receiving the therapy.

TABLE 18a

Scores on the International Index of Erectile Function questionnaire (IIEF-15) – "General Satisfaction" section before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Score
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	3.2 ± 0.6
		During therapy (3 mos)	3.7 ± 1.1
		After therapy (6 mos)	4.4 ± 2.2
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	3.1 ± 0.6
		During therapy (3 mos)	5.2 ± 1.5
		After therapy (6 mos)	7.1 ± 1.8
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	3.2 ± 1.4
		During therapy (3 mos)	5.2 ± 1.8
		After therapy (6 mos)	4.1 ± 1.4
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	2.9±1.4
		During therapy (3 mos)	5.0±1.9
		After therapy (6 mos)	3.9 ± 1.4
5	Placebo	Before therapy	2.8 ± 0.7
		During therapy (3 mos)	2.9 ± 0.5
		After therapy (6 mos)	3.1 ± 0.8

The results reported in Table 18a indicate that the scores on the International Index of Erectile Function questionnaire (IIEF-15) – "Orgasmic Function" section, before, during and after therapy with the combination according to the invention (Group 2); testosterone (Group 1); placebo (Group 5); acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4). The combination according to the invention significantly increased the scores at 3 months ($F = 33.6$, $P < 0.01$) and 6 months ($F = 21$, $P < 0.01$). The administration of testosterone significantly increased the scores at 3 months ($F = 12.6$, $P < 0.01$) but not at 6 months ($F =$

2.3, P = n.s.). The placebo, acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) did not induce any significant changes in score.

These results indicate that testosterone and the combination according to the invention are significantly more active than placebo, acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) in increasing the general satisfaction of patients receiving the treatment. In particular, the combination according to the invention proved significantly more active than testosterone.

TABLE 19a

Scores on the Hamilton Depression Scale questionnaire (DMS III) before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Score
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	6.6 ± 1.0
		During therapy (3 mos)	5.8 ± 0.7
		After therapy (6 mos)	5.1 ± 1.3
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	6.3 ± 1.1
		During therapy (3 mos)	4.7 ± 0.9
		After therapy (6 mos)	3.2 ± 1.1
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	6.7± 1.4
		During therapy (3 mos)	4.8 ± 1.4
		After therapy (6 mos)	5.8± 1.3
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	6.2 ± 1.7
		During therapy (3 mos)	5.4 ± 1.6
		After therapy (6 mos)	5.9 ± 1.6
5	Placebo	Before therapy	6.8 ± 0.8
		During therapy (3 mos)	5.8 ± 0.7
		After therapy (6 mos)	5.5 ± 1.1

The results reported in Table 19a indicate that the scores on the DMS III questionnaire before, during and after therapy with the combination according to

the invention (Group 2); testosterone (Group 1); placebo (Group 5); acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4). The combination according to the invention induced a significant decrease in DMS III scores both at 3 months ($F = 19.2$; $P < 0.01$) and at 6 months ($F = 13.0$; $P < 0.01$). The administration of testosterone induced a significant decrease in DMS III scores at 3 months ($F = 4.07$; $P < 0.05$), but not at 6 months ($F = 2.5$; P = n.s.). The administration of placebo, acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) induced a significant decrease in DMS III scores at 3 months, but not at 6 months. No significant difference was detected between the scores obtained at 6 months with placebo or and testosterone ($F < 1$, P = n.s.), whereas the score obtained with the combination according to the invention was significantly lower ($F = 17.4$; $P < 0.01$).

These results indicate that the combination according to the invention is significantly more active than the other tested compound.

TABLE 20a

Scores on the fatigue scale before, during and after administration of testosterone undecaonate 40 x 2 mg/day (Group 1); propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day (Group 2), acetyl l-carnitine alone 4 g/day (Group 3); propionyl l-carnitine 4 g/day (Group 4) or placebo (Group 5), for 6 months.

Data are mean ± standard deviation.

Group	Type of therapy	Observation time	Score
1	Testosterone undecaonate 40 x 2 mg/day	Before therapy	2.8 ± 1.3
		During therapy (3 mos)	1.1 ± 1.0
		After therapy (6 mos)	0.6 ± 0.4
2	Propionyl L-carnitine 1 x 2 g/day + acetyl L-carnitine 1 x 2 g/day	Before therapy	2.7 ± 1.3
		During therapy (3 mos)	1.3 ± 1.1
		After therapy (6 mos)	0.5 ± 0.4
3	Acetyl L-carnitine 2 x 2 g/day	Before therapy	3.2 ± 2.8
		During therapy (3 mos)	1.4 ± 1.6
		After therapy (6 mos)	2.2 ± 1.8
4	Propionyl L-carnitine 2 x 2 g/day	Before therapy	2.8 ± 1.9
		During therapy (3 mos)	1.2 ± 1.1
		After therapy (6 mos)	2.3 ± 1.9
5	Placebo	Before therapy	2.9 ± 0.8
		During therapy (3 mos)	2.9 ± 0.8
		After therapy (6 mos)	3.0 ± 0.8

The results reported in Table 20a indicate that the scores on the fatigue scale questionnaire before, during and after therapy with the combination according to the invention (Group 2); testosterone (Group 1); placebo (Group 5); acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4). The combination according to the invention induced a statistically significant increase in the scores at 3 months ($F = 12.2$, $P < 0.01$) and at 6 months ($F = 9.3$, $P < 0.01$).

The administration of testosterone induced a statistically significant increase in the score at 3 months ($F = 33.6$, $P < 0.01$) but no significant increase at 6 months ($F = 5.9$, P = n.s.).

Placebo, acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) induced no significant changes in score.

The results presented in Table 20a indicate that testosterone and the combination according to the invention are significantly more active than placebo, acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) in increasing the sensation of general well-being in the patients treated. The best results were achieved with the compound according to the invention.

Unlike placebo, acetyl l-carnitine 4 g/day or propionyl l-carnitine 4 g/day (Groups 3 and 4) both testosterone and the combination according to the invention proved capable of attenuating the symptoms of andropause.

Neither of the compounds tested induced pathological changes affecting the cervico-urethral district. In any event, for testosterone, as mentioned above, its use is still contraindicated in the case of disease of the prostate district as well as for the onset of troublesome adverse effects on the liver, on lipid status, on cardiovascular and prostate diseases, and on sleep and behavioural disorders.

It should be stressed that an important proportion of patients above 50 years of age suffer from diseases of the cervico-urethral district, and therefore cannot be treated with testosterone.

Moreover, the combination of the invention presented high efficacy in the most clinically significant and those involving patients' compliance aspects (see Tables 9a, 12a, 14-20a).

The combination according to the invention may therefore be regarded as the drug of choice in the treatment of patients with symptoms associated with ageing, since, in addition to being more active than testosterone, it can be used in a larger number of patients.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issuing thereon.

date: 13/05/2008

Aleardo Koverech

CURRICULUM VITAE

Name:	Aleardo Koverech
Born:	24 July 1948, Rome
Address:	Via Aurelia Antica, 200 00165, Rome
Qualification:	Graduate in Medicine and Surgery, University of Rome 29 Dec 1978.
Hospital Medicine Experience:	Rheumatology, Gastroenterology, Hematology, General Medicine.
Specialization:	Medical Angiology , University of Catania, 1997. Clinical Pharmacology, University of Catania, 1990.
Employment:	Director, Nutraceutical Products and Strategic Development of Carnitine in Europe, Sigma-Tau Pharmaceuticals .
Experience:	Specific experience in various sectors regarding Hospitals and Universities nationwide, as well as Pharmaceuticals with socialization in Pharmacoeconomics.
Scientific Activity:	- Contractual Professor of PharmacoEconomics at University of Rome. - Professor of Aesthetic Medicine at the International Foundation Fatebenefratelli; Rome.
Since 1980:	Associate Editor of EOS. Journal of Immunology and Immunopharmacology.
Since 1980:	Scientific Director of the Journal – Pharmacoeconomics News Published by CIC.

Some publications:

- L-carnitine fumarate and isovaleryl-L-carnitine fumarate accelerate the recovery of bone volume/total volume ratio after experimetally induced osteoporosis in pregnant mice.
Calcif Tissue Int. 2008 Mar;82(3):221-8.

- Acetyl l-carnitine (ALC) treatment in elderly patients with fatigue.
Arch Gerontol Geriatr. 2008 Mar-Apr ;46 82): 181-90.

- Efficacy and tolerability of combined treatment with L-carnitine and simvastatin in lowering lipoprotein(a) serum levels in patients with type 2 diabetes mellitus.
Atherosclerosis. 2006 Oct;188(2):455-61.

- Acetyl-L-carnitine plus propionyl-L-carnitine improve efficacy of sildenafil in treatment of erectile dysfunction after bilateral nerve-sparing radical retropubic prostatectomy.
Urology. 2005 Nov;66(5):1080-5.

- Placebo-controlled double-blind randomized trial on the use of L-carnitine, L-acetylcarnitine, or combined L-carnitine and L-acetylcarnitine in men with idiopathic asthenozoospermia.
Fertil Steril. 2005 Sep;84(3):662-71.

- L-carnitine and isovaleryl L-carnitine fumarate positively affect human osteoblast proliferation and differentiation in vitro.
Calcif Tissue Int. 2005 Jun;76(6):458-65.

- Carnitine replacement in end-stage renal disease and hemodialysis.
Ann N Y Acad Sci. 2004 Nov;1033:52-66. Review.

- Preliminary observations on the use of propionyl-L-carnitine in combination with sildenafil in patients with erectile dysfunction and diabetes.
Curr Med Res Opin. 2004 Sep;20(9):1377-84.

- Oral propionyl-l-carnitine and intraplaque verapamil in the therapy of advanced and resistant Peyronie's disease.
BJU Int. 2002 Jun;89(9):895-900.

- L-carnitine reduces plasma lipoprotein(a) levels in patients with hyper Lp(a).
Nutr Metab Cardiovasc Dis. 2000 Oct;10(5):247-51.

- Treatment of Mitochondrial Diseases.
Mitochondrial DNA in Human Pathology, edited by S. Di Mauro and D.C. Wallace.
Raven Press, Ltd., New York 1993.

- L-Carnitine: a partner between immune response and lipid metabolism? Mediators of inflammation 2, S29-S32 (1993).
Published By Rapid Communications of Oxford Ltd.

- Carnitine Deficiency in HIV-Infected Subjects: Carnitine Modulates S and G2 - M Phases Lymphocytes.
Annuals New York, Accademy of Sciences 1992.

- Terapia della dispepsia non organica: bilancio critico.
Patologia Gastrointestinale. Recenti acquisizioni terapeutiche G. Dobrilla, G. de Pretis, M. Comberlato (a cura di) Verona.
Bi & Gi Editori. 1992, pp. 21-38.

- Ruolo dei recettori instaminici H3 nel controllo della secrezione gastrica, Simad 5, Atti Monduzzi Editore, 1992.

- Alpha and Beta cell function in hypoglicemic infants of diabetic mothers: clinical implications, Recent advances on hypoglicemic, Raven Press, Volume 89 pp. 291-294, 1992.

- Acetyl-L-Carnitine: a Neuroprotective Therapy for Alzheimer's Disease.
Society for Neuroscience, 21st annual meeting, New Orleans, Louisiana, November 10-15, 1991.

- Safety profile of ofloxacin : the Italian data base
Infection 1986; 14 suppl 4: S 335-7

- In vitro effect of inosiplex on T lymphocytes. Influence on T cells with receptors for IgG (T gamma)
J Immunopharmacolol. 1982;4:139-52.